

REMARKS

Claims 21-31 are currently pending in the application. Applicants presented proposed amendments to Claims 21 and 22 in the response after final Office Action dated September 27, 2002. In the Advisory Action of October 15, 2002, the Examiner declined to enter the amended claims on the grounds that the proposed amendments allegedly raised new issues that would require further consideration and/or search. Specifically, it was noted that recitation in Claim 21 of a protein comprising amino acids 21-401 of SEQ ID NO:2 would require a new search and further consideration. (Applicants note that the claim actually recites amino acids 22-401, not amino acids 21-401).

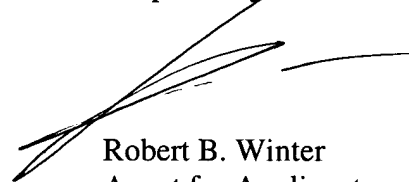
Applicants hereby submit a request for a continued prosecution application (CPA) under 37 CFR 1.53(d). Claims 21 and 22 in amended form are presented herein and entry of the proposed amendments is respectfully requested.

Applicants maintain that Claims 21-31 are patentable for the reasons of record and request that all outstanding rejections be withdrawn.

CONCLUSION

Claims 21-31 are in condition for allowance and an early notice thereof is solicited.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

21. (amended) A protein having a formula selected from the group consisting of R_1 - R_2 and R_1 -L- R_2 , wherein R_1 is a Fc protein, or a variant or fragment thereof, R_2 is a variant or fragment of an osteoprotegerin (OPG) protein comprising amino acids 22-401 as shown in Figure 2 (SEQ ID NO:2) [variant or fragment], and L is a linker, wherein the protein has the activity of decreasing bone resorption.

22. (amended) The protein according to claim 21, wherein the Fc protein is selected from the group consisting of:

- (a) the Fc amino acid sequences as set forth in Figure 1 (SEQ ID NO:1);
- (b) the amino acid sequence of subpart (a) having a different amino acid substituted or deleted in one or more of the following positions (using the numbering according to Figure 1 (SEQ ID NO:1)):
 - (i) one or more cysteine residues;
 - (ii) one or more tyrosine residues;
 - (iii) cysteine at position 5 deleted or substituted with an alanine;
 - (iv) leucine at position 20 deleted or substituted with glutamine;
 - (v) glutamic acid at position 103 deleted or substituted with an alanine;
 - (vi) lysine at position 105 deleted or substituted with an alanine;
 - (vii) lysine at position 107 deleted or substituted with an alanine;
 - (viii) deletion or substitution of one or more of the amino acids at positions 1, 2, 3, 4, and 5;
 - (ix) one or more residues substituted or deleted to ablate the Fc receptor binding site;
 - (x) one or more residues substituted or deleted to ablate the complement (C1q) binding site; and
 - (xi) a combination of subparts i-x;
- (c) the amino acid sequence of subparts (a) or (b) having a methionyl residue at the N-terminus;
- (d) the Fc protein, or variant, fragment or derivative thereof, of any of subparts (a) through (c) comprised of a chemical moiety connected to the protein moiety;

(e) a derivative of subpart (d) wherein said chemical moiety is a water soluble polymer moiety;

(f) a derivative of subpart (e) wherein said water soluble polymer moiety is polyethylene glycol; and

(g) a derivative of subpart (e) wherein said water soluble polymer moiety is attached at solely the N-terminus of said protein moiety.